

Section of Dermatology

President John Franklin MD

Meeting November 21 1963

Cases

Maduromycosis

H W Chadfield MRCPED

W P, male. A negro, aged 51 years

A native of Grenada in the Windward Islands of the West Indies, he has lived in the United Kingdom for the past five years and worked here as a labourer in a foundry until a year ago.

History: Twenty years ago he stumbled on his right foot and this was followed by a painless swelling which remained slight until eight months ago when it increased in size. He states it has never discharged.

At the time of the accident and during the greater part of his life, he was employed in gardening and soil cultivation. He was frequently barefooted.

He first came under my care on 27.6.63.

On examination: General physical condition good. No signs of any systemic disease.

Inguinal glands rather prominent on both sides, but no other adenopathy. A large, deep-seated, non-tender, puffy swelling is present over the entire dorsum of the right foot and toes (except the hallux). It is studded with hard, superficial nodules and deep-seated nodular infiltrations are also present.

Ankle and toe movements are full within the limits imposed by the swelling and he walks reasonably well with a moderate limp.

Investigations: X-ray of right foot: 27.6.63, no bony lesion seen; 12.11.63, moderate degree of osteoporosis, commensurate with disuse, but no bony lesion. X-ray of chest: clear lung fields.

W.R. negative. Haematological investigations within normal limits. Serum proteins normal. Urine normal.

Culture of superficial swab of lesion produced very scanty colonies of *Staph. albus*.

Biopsy: Small black granules seen with the naked eye. Microscopic and cultural studies (utilizing Sabouraud's agar) revealed a maduro-mycotic infection. The specimens were kindly investigated by Dr J C Gentles and Dr S C Tyagi (Department of Bacteriology, University of Glasgow), who isolated *Madurella grisea*.

Treatment and course: Tab. sulphadiazine 4 g daily in divided doses for three weeks without effect. Tab. dapsone 100 mg b.d. for eight weeks without significant improvement. Potassium iodide up to gr 15 t.d.s. with penicillin (twice weekly injections of benethamine penicillin G; procaine penicillin G; sod. penicillin G, and tab. penicillin VK 250 mg q.i.d.) since 28.10.63.

Comment

This case typifies the initial history of trauma, the association with agricultural pursuits, the unshod habit, the painlessness and the very slow and prolonged but nevertheless relentless course appertaining to this 'intermediate' mycosis. The correlation with climatic factors found by Abbott (1956) as epidemiologically significant is also seen, the alternating long rainy and hot dry seasons which occur in the Windward Islands favouring the growth of the fungus and its subsequent sporulation. The absence of sinus formation and of radiological evidence of bone involvement is unusual in a case of this duration but not unknown. Abbott (1956) stated that sinuses may be very late in appearing and that many cases must be diagnosed without them while, according to Arredondo & Ceballos (1962), bony involvement is not always present but will eventually occur unless therapy is promptly instituted.

Four types of onset are usually described, the condition commencing as a small papule, a subcutaneous nodule, a vesicle surmounting a hard swelling or as a small abscess or boil. The causal parasite is an inhabitant of the soil and presumably gains entrance through the skin following

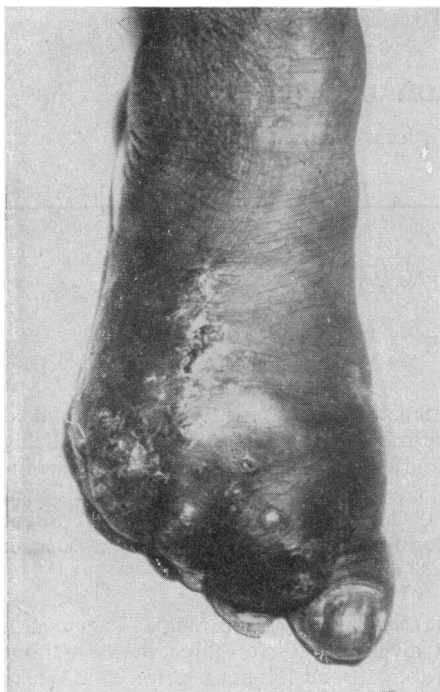


Fig 1 Large swelling involving right foot and toes

trauma. The chronic destructive granulomatous and suppurative infection spreads deeply to involve connective tissue and bone; muscle, nerves and tendons usually resist invasion until the late stages. In the course of time, sometimes after many years, a thickened, deformed, swollen, club-shaped, fibrotic and deeply honeycombed extremity is produced (see Fig 1). While the foot is the most commonly affected organ – and hence the term Madura foot named after Madura in southern India where the disease is prevalent – this disease can affect the hand, the leg, or, less commonly, the trunk or face. Except rarely from gross bacterial secondary infection, systemic effects are not seen and the patient is afebrile. Haematogenous spread does not occur and visceral involvement is very rare but has been described in the brain and the lung. When death results it is from immobility, loss of earning power and neglect.

The discovery of the grains which are compact colonies of the causative organism and their direct microscopical and cultural examination clinches the diagnosis and differentiates this condition from superficially similar diseases like tuberculosis, syphilis, elephantiasis, neoplasia, leprosy, yaws, blastomycosis, chromoblastomycosis, sporotrichosis and coccidioidomycosis.

According to Ainsworth (1952) more than forty organisms classified in a dozen genera have been claimed as being causally related to Madura foot which is to be regarded as a clinical rather than an aetiological entity. The two main classes are (a) the Actinomycetes or bacteria-like fungi which cause the actinomycotic mycetomas (aerobic species are usually involved, differentiating the condition from actinomycosis) and (b) higher fungi, the Fungi Imperfecti or Hyphomycetes, which cause the maduromycoses, and consist of large segmented branched hyphae and frequently spores. This differentiation is of considerably more than academic importance: whereas the Actinomycetes are stated to be susceptible to chemotherapeutic substances, the higher filamentous fungi have hitherto proved completely refractory to such treatment presumably because of the difficulty in penetrating the grain defences. In the former group good results have been claimed from the sulphonamides, broad spectrum antibiotics, carbomycin, chloramphenicol, streptomycin and dapsone.

More recently the aromatic diamidines, e.g. diamidinodiphenylamine dihydrochloride (Abbott 1956) and amphotericin B (used with the isolated limb perfusion technique of Fonkalsrud *et al.*, 1961, because of its toxicity when parenterally administered) have been tried in the hope of influencing especially the Fungi Imperfecti, and *in vitro* sensitivity tests are being planned for this patient. Recent experiments with these substances on mice, however, including *in vitro* sensitivity tests on grains artificially produced in them (Murray & Colichon 1962), give little ground for optimism. Although surgical intervention has apparently hitherto been required in nearly all cases of maduromycosis, it is generally agreed that medical treatment should be given a trial initially in all cases and it may also be of value pre-operatively in controlling secondary infection. Surgery usually implies amputation well above the site of the disease because of the frequency of post-operative recurrence, though some early cases have been dealt with satisfactorily by means of a local excision of the lesion. This case is of long standing, but a surgeon is prepared to attempt a conservative operation. The patient, however, is as yet completely irreconciled to any form of surgical intervention and leaves us no option at present but to persevere with drug therapy.

REFERENCES

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- Ainsworth G C (1952) *Medical Mycology*. London; p 39
- Arredondo H & Ceballos J (1962) *Radiology* 78, 72
- Fonkalsrud E W, Shiner J, Haan R, Marable S A, Newcomer V & Rocklin D B (1961) *Surg. Gynec. Obstet.* 113, 306
- Murray T G & Colichon H (1962) *Trans. R. Soc. trop. Med. Hyg.* 56, 165

Dr Chadfield: The resistance to chemotherapeutic substances encountered in this patient is to be expected from the type of fungus present. I would be glad to hear if anyone has had any personal experience of this condition and would welcome any suggestions as to the further management of this case.

Dr R W Riddell: In a recent world-wide survey of cases of mycetoma it was estimated that about 40% were due to true fungi (Mariat 1963). It is, of course, in this category that Dr Chadfield's case belongs. *Madurella grisea*, the fungus which his mycological adviser suggests is responsible for this black grain infection, is the commonest cause of the disease due to the true fungi in South America. Elsewhere in the world it is less common.

In the 60% of cases of mycetoma not caused by true fungi, Actinomycetes are responsible. These are susceptible to a number of antibacterial type chemotherapeutic agents which would not be expected to be of value in the treatment of mycetomas due to true fungi.

REFERENCE

Mariat F (1963) *Bull. Soc. Pat. exot.* 56, 35

Postscript (22.1.64): The sensitivity tests to griseofulvin and amphotericin B showed that the organism was insensitive to these drugs. The patient finally consented to undergo operation and the tumour was dissected out on 13.1.64 with the sacrifice of only a few tendons on the dorsum of the foot. It is planned to undertake grafting at a later date.—HWC

Angiokeratoma Corporis Diffusum

IS Hodgson-Jones MD MRCP

A K, female, aged 30. Italian, married

History: Rash on buttocks appeared four years ago and slowly spread. She also complained of lethargy and hiccup. She had had no previous illnesses.

General physical examination: Angiomatous and keratotic papules on buttocks and right arm. Cardiovascular system normal. Blood pressure 120/80. Alimentary system: liver and spleen impalpable. Respiratory and central nervous systems normal.

Investigations: Blood count and plasma proteins normal. ESR (Wintrobe) 25 mm in one hour, corrected for PCV of 39% to 15 mm. Urine: sterile pyuria. Culture: *Myco. tuberculosis* grown. Blood urea 26 mg/100 ml.

X-rays: Chest: calcification of both hilar and mid zones; healed primary tubercle; heart shows no enlargement. IVP: left hydronephrosis. Bones of

hands normal. Cervical spine: C.4, 5 and 6 show flattening and double-contoured vertebral bodies.

Eyes: Slit-lamp examination shows that the substantia of the cornea is rather mottled in the central area, although the changes seen were thought to be those not uncommonly seen in normal subjects. No corkscrewing or beading of the retinal veins. No wedge-shaped opacities or mustard-tinted veiling. Visual acuity and fields normal.

Biopsy: Thin-walled cavernous angiomatous spaces high in the dermal papillae, associated with acanthosis and hyperkeratosis of the overlying epidermis.

Comment

Unfortunately no opportunity has arisen to examine any other members of her family, as they live in Italy, but so far as can be ascertained none suffers from this complaint.

The numerous systemic associations of this disease have been reviewed by Wise *et al.* (1962). They stress the extreme rarity of the condition in women and suggest that this is because it is a sex-linked genetic abnormality with only occasional penetrance in the heterozygous female.

There were no conclusive eye changes, but this is an early case and it is possible that further opacities will occur later.

The finding of double-contoured vertebral bodies in the cervical spine has been described previously in this condition. It is a very rare abnormality and is unlikely to be a fortuitous finding unconnected with the skin changes.

In the course of investigations it was found that this patient had renal tuberculosis. She has received medical treatment for this with apparently successful results, but without any alteration in the skin lesions.

REFERENCE

Wise D, Wallace H J & Jellinek E H
(1962) *Quart. J. Med.* 31, 177

Dr D Wise: There has been little change in the lesions of this woman with widespread angiokeratoma since Dr Hodgson-Jones kindly showed her to me three years ago. The present patient differs from the five women I have seen with clustered skin lesions due to hereditary diffuse angiokeratoma. The main points of distinction are that the present patient has a very florid eruption with profuse, large lesions and obvious hyperkeratosis, whereas the hereditary disorder in